"This was almost certainly postdated; probably the illness, whatever it was, caught up with Goya in Andalusia sometime before, when he was staying with a friend in Cadiz named Sebastian Martinez. It was the last letter Goya would write for some time. No one can say what laid him low and so nearly killed him. He heard loud and constant noises, buzzing and roaring and ringing, in his head. But he had more and more difficulty hearing the sounds of the real world, and he could hardly make out syllables of ordinary speech. His balance was badly affected; he could not go up and down stairs without feeling in danger of falling over. He had fainting fits and spells of semi-blindness. As happens with disturbances of equilibrium, he often felt nauseated and ready to throw up. Gradually the more humiliating symptoms receded, but from 1793 onward after he turned forty-six, Goya would be functionally deaf. (Hughes, Robert. *Goya*. London: The Harvill Press, 2003:127

The significant problem of visual field contraction as the result of the use of vigabatrin, an anti-epileptic, is now well recognised. Regrettably, this drug is especially effective in certain childhood seizures that are resistant to other mainstream medications. The full impact of this problem is summarised by Hardus and coworkers in a study of 11 patients with 4 years of follow up in the Netherlands. This study demonstrates that the abnormalities of EOG/ERG and visual field function do not improve over a relatively long period of time after the vigabatrin has been discontinued. It would appear that the retinotoxic effect of this drug is permanent and early detection is mandatory in order to avoid significant visual loss. (*Acta Ophthalmol Scand* 2003;**81**:459–65)

Some of the findings of the human genome project are very surprising. Geneticists have long focused on just a small portion of DNA that contains the blueprints for proteins. These were felt to be the sole mainspring of heredity and they were the complete blueprint for life. However, it now appears that this is not correct. The remaining 98% of DNA in humans that was previously dismissed as junk now appears to have important roles. Many hidden genes appear to work through RNA rather than protein and this has overturned our previous understanding. These RNA-only genes tend to be short and difficult to identify. But some of them have major roles in the health and development of plants and animals. Active forms of RNA also help regulate a separate epigenetic layer of heritable information that resides in the chromosomes but outside the DNA sequence. The field of genetics is becoming more complex as scientists investigate what was once considered to be junk DNA. (*Scientific American* 2003;**289**:47–51)

Carpal tunnel syndrome is a common disorder for which several conservative and surgical options are available. Many patients prefer to splint the involved wrist in order to avoid surgical intervention. Splinting is not successful in all patients. In a study from Amsterdam where patients were randomised in a controlled study, one study group wore a wrist splint for 6 weeks at night. Others were randomised to surgical intervention. This study revealed that approximately two thirds of splinted patients reported improvement. Prognostic factors that helped predict improvement were the duration of symptoms. Those who had paraesthesias for shorter periods of time were likely to be more successful with splinting. At least in the short term, splinting seems to be a reasonable alternative to surgical intervention in the treatment of carpal tunnel syndrome, as long as motor nerve function has not been compromised. (*J Neurol Neurosurg Psychiatry* 2003:1342–4)

The evidence is conflicting as to whether an inflammatory process is important in the evolution of Alzheimer's disease. It has been known for some time that patients who regularly take anti-inflammatory drugs appear to have less risk of developing the disease. Some have hypothesised therefore that the Alzheimer brain is actually inflamed and that damage occurs when microglia, the brain's immune cells, become overactive and attack healthy neurons. New research however opposes this view. In this view microglia simply age, lose their ability to protect the brain and to prevent the progressive deterioration of neurons and deposition of β amyloid protein. This research emphasises that keeping the ageing microglia healthy may be the primary focus for future forms of Alzheimer's therapy. Opinion may be swinging away from the notion that inflammation is an important process in Alzheimer's disease and that routine anti-inflammatories are protective for this disease. (*JAMA* 2003;**213**:110)

It is estimated that 100 000 deaths each year in the United States occur as a result of adverse reactions to prescription drugs. This is not all the result of physician error. Moreover, many millions of people are being treated with drugs that will never do much good for them. For example, β blockers, given to reduce blood pressure, will be ineffective in at least one third of patients. Some antidepressants work in less than half of the patients who take them. This problem is primarily related to the genes which help to determine the way in which the human body reacts to drugs. Small genetic variations between people, polymorphisms, can alter the behaviour of proteins that carry a drug to its target cell or tissue, cripple the enzyme that activates a drug or aid its removal from the body, or alter the structure of the receptor to which a drug is supposed to bind. Investigators have now identified a key group of drug metabolising enzymes known as the p450 family. These enzymes are produced in the liver and oxidise foreign chemicals. Of the 57 genes for the p450 enzymes that have been identified in humans, three are particularly important for drug metabolism. A new field is developing called pharmacogenomics. These scientists envision the day when a physician would send off a blood sample for analysis and get back a ranked list of the best options of drugs available for that patient's genetic system. (*Nature* 2003;**425**:760–2)

"The research process itself is also immersed in a financial quagmire of conflicts of interests. A recent study at the University of California San Francisco found that a third of faculty investigators received payments from companies for delivering lectures and accepting consultancies. Ownership of shares in pharmaceutical companies and personal financial ties are common. Prestigious medical conferences organised by some of the world's most respected specialist societies—such as the European Society of Cardiology—are now packed with industry sponsored symposiums promoting a product, a company, or both. There is, more than ever, convincing evidence that in some cases the opinions of medical experts can be bought by the highest bidders. Doctors who take money from drug companies are more likely to sing the company line—hiding anxieties about safety—than those who keep their hands firmly in their pockets. Such is the atrocious venality of modern academic medicine." (Horton, Richard. *Health Wars on the Global Front Line of Modern Medicine.* New York: New York Review of Books 2003:300)